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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,607	12/09/2003	Keith Roger Bley	R0032H-DIV	4763

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EXAMINER	
MORRIS, PATRICIA L	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,607	BLEY ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-83* is/are pending in the application.

4a) Of the above claim(s) *74-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66,69 and 70* is/are rejected.

7)☒ Claim(s) *67,68 and 71-73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 66-73 are under consideration in this application.

Claims 74-83 are held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b).

Election/Restrictions

Applicants' election of Group III and the species of example 18 with traverse in the reply, filed April 27, 2005, is acknowledged. The traversal is on the grounds that the examiner has improperly characterizes claim 74 as a combination therapy claim. This is not found persuasive for the reasons clearly set forth in the previous Office action. The examiner is well aware of what a composition claim consists of. Applicants' own composition claims states "treatment with an **AP receptor antagonist, which composition comprises as an ingredient**". It is clear that applicants intend other ingredients. If applicants' arguments were presumed to be correct, claim 74 is clearly not in proper form. Further, applicants have failed to advance any cogent reasons as to why the inventions are not patentably distinct. It is proper to restrict out the multiple uses. Note MPEP 806.05(h).

The restriction requirement is deemed sound and proper and will be maintained.

This application has been examined with regard to the elected compound wherein R^1, R^8 and R^9 represent nonheterocyclic containing groups and R^1, R^2 ,R^4 and X as set forth in claim 1, exclusively.

Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 66, 69 and 70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is a lack of description as to whether the compounds are able to be maintained in all the unknown crystal forms. Processing a compound into a pharmaceutical composition could create a different crystalline form than the forms being claimed or even back to the compound itself. See pages 912-913 of Habeblian. Jain et al., pages 322-326 teach that manufacturing processes affect polymorphs. Taday et al. on page 831, teach "..Once in the desired crystalline form, the polymorphic state may be changed by incorrect storage or even during tablet preparation". Doelker et al. Abstract, "One may also observe changes in technology or pharmaceutical properties that are due to polymorphic environmental conditions undergone by the product or dosage form." The specification fails to describe the crystalline forms for any of the elected compounds claimed in terms of their X-ray diffraction pattern or infrared spectrum data.

Chemical & Engineering News discloses that formulation of drugs or pharmaceuticals in its metastable forms, for example, one polymorph, is highly unpredictable. The metastable forms will disappear and change into the most thermodynamically stable form. The specification lacks description of how the pharmaceutical composition can be prepared in order to maintain the particular compound of a particular form with the particular infrared spectra and X-ray

diffraction being claimed. Disclosure of X-ray diffraction patterns for the elected compounds comprising crystalline forms are lacking in the specification. The specification has also not described how the crystalline being claimed will be maintained and prevented from converting to other forms. Jain et al.., p 322-326, recite the manufacturing processes that affect polymorphs. Otsuka et al. On page 852 states « in formulation studies and the method preparing CBZ has been shown to affect the drug's pharmaceutical properties through the polymorphic phase transformation of the bulk CBZ powder during the manufacturing process".

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of novel crystalline forms of the instant compounds.

State of the Prior Art

Crystals arise when molecules of a compound stack in the solid state in distinct ways. (See Chemical Engineering News, page 32). Although identical in chemical composition, crystalline forms can have very different properties. They are distinguishable by various analytical techniques, especially X-ray powder diffraction. Additionally, solids may form solvates. Crystalline forms tend to convert from less stable to more stable forms. (See Chemical Engineering News, page 32). No method exists to predict the crystalline forms of a solid compound with any significant certainty. In drug design, it is best work with the most stable crystal, because it will not covert any further, however, the most stable crystalline form usually is the least soluble. To improve bioavailability, drug companies sometimes trade off crystalline stability with solubility, choosing to work instead with the less stable forms first, also known as the metastable forms. Crystalline forms can convert from one form to another during the manufacturing process of a pharmaceutical drug. See Chemical Engineering News. Page 33, which will changed the pharmacological affects of the drug. This is why it is important to monitor the crystalline form during manufacture of the drug to see if it persists during manufacture.

The amount of direction or guidance and the presence or absence of working examples

The specification fails disclose the X-ray diffraction pattern and IR spectrum data of the crystalline forms being claimed. Crystalline forms often change into other polymorphs during drug manufacture (See Chemical Engineering News) into a pharmaceutical composition.

The breadth of the claims

The breadth of the claims are drawn to the all unknown crystalline forms and in addition to the claimed compounds.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the crystalline forms being claimed and verifying that they have the specific X-ray diffraction patterns being claimed which are not disclosed in the specification.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 66, 69 and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression crystal form in claims 66, 69 and 70 is indefinite to its meaning. What are the intended crystal forms?

The expression R^6 is absent when X is S or O in claim 66 appears to be no longer necessary.

The claims measure the invention. United Carbon Co. V. Binney & Smith Co., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, AClaims measure invention and resolution of invention must be based on what is claimed.

The C.C.P.A. in 1978 held a that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim. In re Priest, 199 USPQ 11, at 15.

Drawings

The formal drawings filed on December 9, 2003 have been accepted.

Applicants are requested to update the status of all the parent applications on page 1, line 1 of the specification. Cooperation herein is appreciated.

Allowable Subject Matter

Claim 66 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112 set forth in this Office action and if rewritten directed solely to the elected compounds.

Claims 69 and 70 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of

the base claim and any intervening claims and if rewritten directed solely to the elected compounds.

Claims 67, 68 and 71-73 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and if rewritten directed solely to the elected compounds.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia L. Morris
Primary Examiner
Art Unit 1625

plm
June 23, 2005